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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BASQUILL, SEAN M	

ART UNIT	PAPER NUMBER
1612	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/579,042	LEE ET AL.	
	Examiner	Art Unit	
	Sean Basquill	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10 May 2006; 29 Jan 2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Claims 1-16 directed to compounds of Formula I having a piperidine core in the reply filed on 11 May 2010 is acknowledged. The traversal is on the ground(s) that the compounds of Formula I as claimed have common utility as melanocortin receptor agonists and that the compounds share a common structural feature essential to that utility. This is not found persuasive because of the reasons put forth in the restriction requirement mailed 12 April 2010. To reiterate, owing to the diversity of the core structure claimed as the compound of Formula I, the examiner asserted that the core encompassed by the compounds as claimed was sufficiently varied, containing as it does three chemically distinct heterocyclic moieties in the core of the compound as claimed.

The requirement is still deemed proper and is therefore made FINAL.
Applicants further elected as the species representative of the invention claimed the compound where substituents R1 and R1 are hydrogen, R3 is 4-chlorobenzyl, R4 is cyclohexyl, and R5 is C(O)CH(Me)2.

Claims 17-20 have been withdrawn as directed to nonelected inventions. Claims 1-16 are presented for examination.

As a threshold matter, the examiner considers the recitation of Claim 16 which states "an agonistic composition of melanocortin receptor" to be a recitation of a property inherent to the active compound contained in the composition therein described. As such, the examiner has afforded it no patentable weight in relation to the affirmatively recited components of the

composition claimed, namely a compound as described in Claim 1 in combination with a pharmaceutically acceptable carrier. This interpretation should be read into the rejections which follow.

Priority

2. Applicant's claims for the benefit of the prior-filed International application PCT/KR04/02929 and Korean National Applications 10-2003-0079799 and 10-2004-0065820 under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) are acknowledged.

Information Disclosure Statement

3. The information disclosure statement filed 10 May 2006 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. While it is true that the references listed on said IDS were made part of the international search report, and are listed thereon, such a listing does not satisfy the requirements of a proper information disclosure statement unless actual copies of the references cited are provided, either by applicants or by the International Bureau. MPEP § 609.03.

Claim Rejections - 35 USC § 112 First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 6-14, and 16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The disclosure as originally filed lacks adequate written description to support claims directed to particular arrangements of variable substituents R1 and R2, as well as certain particular arrangements of variable substituents R4 and R5. Specifically, those claims encompassing piperadine-cored compounds where R1 and R2 are joined to form an optionally substituted 4-8 membered ring optionally containing heteroatoms selected from O, S, and N, and compounds where R4 and R5 are joined to form an optionally substituted 4-8 membered ring optionally containing heteroatoms selected from O, S, and N does not find support in the description as originally filed.

The first paragraph of 35 USC 112 requires that the specification contain a written description of *the invention*. Accordingly, where a particular compound has not been *specifically* named or "otherwise exemplified," one is left to select from mere *possibilities* encompassed by the broad disclosure, with no guide indicating or directing that this particular selection should be made rather than any of the many others which could also be made. *In re Ruschig*, 154 USPQ 118, 122 (CCPA 1967). As elaborated by the court:

> Specific claims to single compounds require reasonably specific supporting disclosure and while we agree with the appellants, as the board did, that *naming* is not essential, something more than the disclosure of a class of 1000, or 100, or even 48, compounds is required. Surely, given time, a

> chemist could name (especially with the aid of a computer) all of the half million compounds within the scope of the broadest claim, which claim is supported by the broad disclosure. This does not constitute support for each compound individually when separately claimed. (*Id.*)

Here, the instant claim broadly recites a compound which is only nominally identified by the terms above, but not specific structures. The only compounds particularly described by the instant specification are those set forth at pages 72-74 (examples 105-161) and pages 80-81, examples 285-293; no others are "specifically named or otherwise exemplified." Accordingly, portions of the claimed subject matter as described above are not adequately described by the specification as originally filed.

5. Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. *See*, e.g., *In re Wilder*, 22 USPQ 369, 372-3 (Fed. Cir. 1984) (holding that a claim was not adequately described because the specification did 'little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate').

Mere indistinct terms such as "derivatives," "solvates," or "isomers" used herein, as well as "heterocycle," "aryl," "heteroaryl," "alkyl,' and the above generic terms modified by their coupling with additional chemical structures, however, may not suffice to meet the written description requirement. This is particularly true when a compound is claimed in purely

functional terms. *See Univ. of Rochester v. G.D. Searle*, 69 USPQ2d 1886 (CAFC 2004) at 1892, stating:

> The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. (Emphasis added).

Conversely, a description of a chemical genus will usually comprise a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *See Univ. of Calf. V. Eli Lilly*, 43 USPQ 2d 1398, 1406 (Fed. Cir. 1997). This is analogous to enablement of a genus under Section 112, ¶ 1, by showing the enablement of a representative number of species within the genus.

A chemical genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. *If the genus has substantial variance, the disclosure must describe a sufficient number of species to reflect the variation within that genus*. See MPEP 2163. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any *combination of such identifying characteristics that distinguish the claimed invention from other materials* and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. MPEP 2163.

Here, the specification does not provide a reasonably representative disclosure of useful derivatives, solvates, or isomers of the compounds or functional moieties of the claimed compounds generally, a potentially huge genus inclusive of many different compounds having potentially widely divergent structures and functions. No description of such modifications reasonably representative of the genus in its claimed scope has been provided because no readily apparent combination of identifying characteristics is provided. The description provided, then, describes generically modifications which would serve to operate as derivatives, solvates, or isomers. It is well recognized that a description by function alone does not suffice to sufficiently describe an invention because it is only an indication of what the claimed invention does, rather than what it is. MPEP § 2163(II)(A)(3)(a), *citing Regents of the University of California v. Eli Lilly, Inc.*, 119 F.3d, 1559, 1568(Fed. Cir. 1997). An adequate written description of a chemical invention requires a precise definition, such as by structure, formula, chemical name, or physical properties. *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927 (Fed. Cir. 2004).

In addition, as currently claimed, the terms "heterocycle," "aryl," "heteroaryl," "alkyl,' and the above generic terms modified by their coupling with additional chemical structures provide no limiting definition as to the size, extent of modification, or heteroatoms which may be included in the structures generically claimed. These define gargantuan, if not infinite genera, which no listing of species could hope to exemplify. The examiner suggests limiting the size of the aforementioned generic descriptions by placing chain or ring size limitations on such descriptive terminology.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-9 and 16 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by U.S. Patent 6,750,348 (hereinafter "Bridger").

Bridger discloses compounds AMD7131, AMD 7198, AMD7272 and AMD7273, as well as pharmaceutical compositions containing the aforementioned compounds, which anticipate the instant claims. (Drawings pg.1, 12, 28, 29, Claims 14 and 15).

7. Claims 1-9, 12, 13, and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Alan R. Jacobson, *et al*, *Minimum-Structure Enkephalin Analogues Incorporating L-Tyrosine, D(orL)-Phenylalanine, and a Diamine Spacer*, 32 J MED. CHEM. 1708 (1989) (hereinafter "Jacobson").

Jacobson describes compounds 8a and 8B, which anticipate the instant claims 1-9, 12, and 13. (Pg. 1709). In addition, Jacobsen describes compositions containing compounds *a and b in distilled water, which the examiner contends is a pharmaceutically acceptable carrier. (Pg. 1717).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 1-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,495,715 (hereinafter "Hu"), in view of George Patani and Edmond LaVoie, *Bioisosterism: A Rational Approach in Drug Design*, 96 CHEM. REV. 3147 (1996) (hereinafter "Patani").

Hu describes a variety of phenyl substituted amino compounds, referred to generally as "Compounds of Formula I." Abs. These compounds contain a number of variable substituents, particularly R^{2-5}, Z, X, V, and Q. (Id.). While a number of possible substituents for each variable are provided, in numerous locations throughout the disclosure Hu indicates certain moieties are preferred for certain variable substituents. Specifically, in multiple locations, Hu indicates that [4,N]-disubstituted piperadine is the preferred moiety for substituent X, and a carbonyl moiety is the preferred substituent for variable Z, reading on the instant claims

recitation of the N-substituted keto piperadine. (C.2, L.60 – C.3, L.50; C.8, L.37 - C.9, L.35). Similarly, in multiple locations throughout the disclosure Hu indicates a dihydrogen substituted amine is the preferred configuration for NR^3R^4, which reads in the preferred amino configuration of the instant claims. (C.3, L.5-8; C.8, L.54). Hu further indicates that preferred moieties for the variable substituents V and Q are to be selected from substituted methoxy, substituted ethyl, or substituted aminomethyl, where the substituents are selected from C_{1-8} alkyl, which represents a chemical homolog[1] of the instantly claimed amino, methoxy, and methyl phenyl substituents R^4. (C.3, L.64-67). Hu additionally indicates that the therein described R^2 substituent can be selected from substituted C_{1-8} alkyl, including the $C(O)R^8$ of the instant claimed invention, and the R^5 substituent can be selected from a group which includes substituted benzyl, corresponding to the substituted benzyl moiety at R^3 of the instant claims. While Hu does not particularly indicate that para-chloro benzene would fall within the subtituted benzene groups within the scope of the Hu disclosure, Patani indicates that chloro substitution is a common method of modifying known compounds to alter metabolic profiles. (Pg. 3154). Finally, Hu indicates that the compounds of Formula I may be mixed with pharmaceutically acceptable excipients for form pharmaceutical compositions. (C.7, L.61-63).

The specific combination of features claimed are therefore disclosed within the preferred embodiments of the substituents taught by Hu, but such "picking and choosing" within several variables does not necessarily give rise to anticipation. *Corning Glass Works v. Sumitomo Elec.*,

[1] When chemical compounds have "very close" structural similarities and similar utilities, without more a *prima facie* case may be made. *In re Wilder*, 563 F.2d 457 (CCPA 1957). Stated alternatively, obviousness may be based solely upon structural similarity (an established structural relationship between a prior art compound and the claimed compound, as with homologs). *In re Duel*, 51 F.3d 1552, 1559 (Fed. Cir. 1995). The necessary motivation to make the claimed compound, and thus the *prima facie* case of obviousness, arises from the reasonable expectation that compounds similar in structure will have similar properties. *In re Gyurik*, 596 F.2d 1012, 1018 (CCPA 1979)

868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of variable substituents as described above as corresponding to the arrangement of moieties as claimed in the instant application, anticipation cannot be found.

That being said, however, it must be remembered that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious." *KSR v. Teleflex*, 127 S.Ct. 1727, 1740 (2007) (quoting *Sakraida v. A.G. Pro*, 425 U.S. 273, 282 (1976)). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious," the relevant question is "whether the improvement is more than the predictable use of prior art elements according to their established functions." (*Id.*). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *KSR* at 1741. The Court emphasized that "[a] person of ordinary skill is… a person of ordinary creativity, not an automaton." *Id.* at 1742.

Consistent with this reasoning, it would have obvious to have selected various combinations of various variable substituents as described above as corresponding to the arrangement of moieties as claimed in the instant application from within a prior art disclosure, to arrive at compositions "yielding no more than one would expect from such an arrangement." As such, the instant application's claimed compounds and pharmaceutical compositions

Conclusion

While no claims are allowable as currently presented, the examiner notes that the compound selected by the applicants as their elected species, where R1 and R2 are hydrogen, R3 is *para*-chloro benzyl, R4 is cyclohexyl, and R5 is C(O)(CH(Me)2 is free of the art, and would be allowable if specifically and particularly claimed. Applicants are encouraged to contact the examiner to discuss the status of the case, and appropriate courses to overcome the rejections of record by an appropriate narrowing of the claims to limit their scope to allowable subject matter.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean Basquill whose telephone number is (571) 270-5862. The examiner can normally be reached on Monday through Thursday, between 8AM and 6PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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